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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,942	02/18/2000	Jean-Marc Balloul	032751-027	9626

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FOLEY, SHANON A

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/506,942	Applicant(s) BALLOUL ET AL.	
	Examin r Shanon Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-38,40,43,44,46-72 and 74-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-38,40,43,44,46-72 and 74-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant amended claims 32, 40, 44, 48-51, 53, 57, 58, 65, 74-77, cancelled claims 39, 41, 42, and 73 in paper no. 16. Claims 32-38, 40, 43, 44, 46-72, and 74-80 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-38, 40, 43, 44, 46-47, 52-58, 65-72, and 74-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 32, 44, and 65 have been amended to a composition "consisting of" certain papillomavirus polypeptides. However, claims 43, 52, and 78, respectively, state that the "composition of claim 32 [44, 65], further "comprises" a pharmaceutical carrier. The discrepancy between what is encompassed in the composition narrowly "consisting of" only certain ingredients, while "comprising" other ingredients renders claims 32/43, 44/52, and 65/78 unclear as to what is in the compositions. The claims are rendered further indefinite because while the composition is "consisting of" certain ingredients, the composition also comprises an indeterminate amount of vectors, i.e. "one or more", in which the various polypeptides are expressed. Therefore, it cannot be determined which specific elements the claims "consist of". See the MPEP 2111.03 and *In re Gray*, 53 F.2d 520, 11 USPQ 255 (CCPA 1931; *Ex Parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("consisting of" defined as "closing the claim to the

inclusion of materials other than those recited except for impurities ordinarily associated therewith."). This rejection also affects claims 53-56 and 59-64.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 32-34, 40, 43, 53, and 54 are rejected under 35 U.S.C. 102(e) as being anticipated by Stanley (US 6,096,869) for reasons of record.

Although applicant has amended the claims to narrow the scope to recite, "consisting of", the ingredients of the composition are indefinite because of the composition "further comprising" additional ingredients in dependent claims. Since it cannot be determined specifically which ingredients are in the composition, the composition of Stanley et al. anticipates the instant claims even though the composition of Stanley et al. is not limited to the papillomavirus proteins recited in the patent. The specific elements recited are anticipated by the teachings of Stanley et al. because the compositions in the reference "comprise" all compositions merely "consisting of" individual elements. Therefore, the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-36, 43, and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galloway (Infectious Agents and Disease. 1994; 3 (4): 187-193), Borysiewicz et al. (The Lancet. June 1, 1996; 347: 1523-1527), and Lin et al. (Virology. 1992; 187: 612-619).

As discussed above, it cannot be determined which ingredients are encompassed by the composition of claims 32, 43, 44, 52-56, and 59-64. However, in order to expedite prosecution, this new rejection set forth under 35 USC § 103 is directed to the narrow claim language drawn to the composition "consisting of" only the ingredients recited in the claim since it is presumed that this is what applicant intended in the amendment to the claims.

The claims are drawn to a composition consisting of one or more recombinant vaccinia vectors, encoding E6, E7, L1, and L2 polypeptides from a papillomavirus that is used to treat papillomavirus infection. The vaccinia vector is a Wyeth strain and expression of the polypeptides is under control of the 7.5K promoter.

Borysiewicz et al. teaches a Wyeth strain vaccinia virus encoding papillomavirus polypeptides E6 and E7 under the control of the 7.5K promoter to treat cervical cancer, see the abstract and "Vaccination with TA-HPV and patient monitoring" section on page 1524. Borysiewicz et al. does not teach expressing the L1 or L2 proteins.

However, Lin et al. teaches protecting rabbits by immunization with vaccinia virus expressing the L1 protein or a plasmid expressing L1 and L2, see the entire document.

One of ordinary skill in the art at the time the invention was made would have been motivated to express L1 and L2 in the vaccinia vector of Borysiewicz et al. or E6 and E7 in the vaccinia vector of Lin et al. to obtain protection and treatment capabilities from the vaccine composition. One would have been motivated to combine the polypeptides into one composition to administer the same composition to those who need treatment and those who need protection. One of ordinary skill in the at the time the invention was made would have had a reasonable expectation for producing the composition because the composition of Borysiewicz et al. expressing the early papillomavirus polypeptides treats infected patients and the composition of Lin et al. expressing the late polypeptides prevents disease. Galloway teaches further evidence of expectation of success in combining the instant polypeptides. The reference teaches that the late polypeptides are prophylactic and the early polypeptides have are therapeutic, see the abstract. Therefore, one of ordinary skill in the art at the time the invention was made would not only had a reasonable expectation for producing the claimed invention, but would have had a reasonable expectation for producing the instant invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 44, 46, 48, 52, 59-62, 65-69, 72, 74, 78-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. Galloway, Borysiewicz et al., and Lin et al. as applied to claims 32-36, 43, and 53-56 above, and further in view of Hines et al.

The claims are drawn to a composition consisting of recombinant vaccinia (Wyeth strain) vectors encoding E6, E7, L1, L2, and IL-2 to treat or prevent papillomavirus infection.

See the teachings of Galloway, Borysiewicz et al., and Lin et al. None of the references teach or suggest administering IL-2 with the recombinant vaccinia vectors expressing E6, E7, L1 and L2 to treat and prevent papillomavirus infections.

However, Stanley et al. teaches a pharmaceutical treatment composition comprising IL-12 and at least one papillomavirus protein, E1, E2, E4, E5, E6, E7, L1, and/or L2 of HPV-16 in a vaccinia expression vector that is used to treat papillomavirus infections, lesions, and neoplasia, see column 2, line 56-column 3, line 2, and claims 1, 2, 5, 6, 10-13. Stanley et al. does not teach administering IL-2.

However, Hines et al also teaches cell adoptive therapy treatment to accelerate tumor regression by stimulating their lymphocytes *in vitro* with a peptide, E6 and E7, and a cytokine, IL-2, which is returned to the cancer patient as therapy, see the "cellular adoptive therapy" section on page 862-863 and figure 2 on page 863.

One of ordinary skill in the art at the time the invention was made would have been motivated to express IL-2 of Hines et al. in the vaccinia expression vectors of Borysiewicz et al. and Lin et al. to stimulate a cellular immune response against papillomavirus tumor formation *in vivo* to eliminate the time-consuming step of extracting, stimulating, and re-administering peripheral blood lymphocytes (PBMC) back into patients. Also, administering the IL-2 in the vector form would eliminate the possibility of contaminating the patient's PBMC before re-administration. One of ordinary skill in the art would be further motivated to express IL-2 in the vaccinia expression vectors of Borysiewicz et al. and Lin et al. to control the amount of

expression of the cytokine and to increase opportunities for the cytokine stimulate more T cells than would be possible to isolate from a single extraction for ex vivo stimulation in culture. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Stanley et al. teaches how one expresses a cytokine in a vaccinia vector in a papillomavirus treatment composition.

Applicant asserts that the Office must demonstrate motivation for one skilled in the art to combine the references and that the Office must also show expectation for producing the claimed invention and that the references teach every limitation in the claims. Applicant specifically argues that the motivating factors for combining the teachings of Hines et al. into the composition of Stanley et al. are purely hypothetical and there is no evidence that suggests that potential problems may arise. Applicant further argues that Hines et al. teaches away from the claimed invention because the reference seems to stress in vitro stimulation of lymphocytes is more effective than in vivo stimulation by the host. With respect to the teachings of Stanley et al., applicant argues that Stanley et al. does not teach the specific combinations of papillomavirus polypeptides recited in the amended claims and that the skilled artisan would have no motivation to express IL-2 of Hines et al. instead of IL-12 in the compositions of Stanley et al. because the patterns of expression of IL-2 and IL-12 are different in the tables of Stanley et al.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art (emphasis added). See *In re Fine*, 837

F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, there is not just one motivating factor for combining IL-2 of Hines et al. in the vaccinia compositions of Borysiewicz et al. and Lin et al., but several. One of ordinary skill in the art at the time the invention was made would have been motivated to express IL-2 in the vaccinia expression vectors of Borysiewicz et al. and Lin et al. to control the amount of expression of the cytokine and to increase opportunities for the cytokine stimulate more T cells than would be possible to isolate from a single extraction for *ex vivo* stimulation in culture. Other motivating factors may be hypothetical, such as time efficiency, but are motivating necessities to one of ordinary skill. Further motivation is drawn from natural inclinations of the ordinary artisan to efficiently and specifically stimulate as many T cells *in vivo* against a papillomavirus infection as possible.

In addition, it is determined that the teachings of Hines et al. are broader than applicant's interpretation. In the phrase recited by applicant, Hines et al. is discussing the immune response to direct administration of viral antigens only and not the additional administration of a cytokine. Hines et al. teaches that the extracted lymphocytes are stimulated with the peptides and the cytokines (emphasis added), which activates the cytotoxic T lymphocytes, see the same section recited by applicant and figure 2 on page 863. Therefore, the teachings of Hines et al. establishes that cytokines, i.e., IL-2, activates cytotoxic T cells. One of ordinary skill in the art at the time the invention was made would have been motivated to express IL-2 in the vaccinia compositions of Borysiewicz et al. and Lin et al. to ensure activation of cytotoxic T cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Stanley et al. teaches expressing a cytokine in a

vaccinia vector to stimulate T cells in order to reduce HPV-induced tumors and Hines et al. teaches that the cytokine IL-2 is a natural stimulator of cytotoxic T cells used to treat papillomavirus infection. Therefore, the Office has met the three criteria to demonstrate a prima facie obvious case in the instant invention. The combination of references not only teach all of the required elements in the claims, but also demonstrate several motivating factors for combining the teachings to produce success once combined.

Applicant has not demonstrated surprising results with the claimed combination. The teachings of Stanley et al. and Hines et al. demonstrate treatment using papillomavirus polypeptides in combination with a cytokine. Although they are different cytokines, they both stimulate cytotoxic T cells and a Th1 response. Therefore, to substitute one cytokine for another in the vaccinia composition of Stanley et al. or express the cytokine in the vaccinia compositions of Borysiewicz et al. and Lin et al. would be obvious to one of ordinary skill in the art, without unexpected results. Therefore, it is maintained that the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. Galloway, Borysiewicz et al., Lin et al. and Hines et al. as applied to claims 32-36, 43, 44, 46, 48, 53, 52-56, and 59-62 above, and further in view of Gajewski (Journal of Immunology. 1996; 156: 465-472).

See the teachings of Stanley et al. Galloway, Borysiewicz et al., Lin et al. and Hines et al. above. None of the references teach administering B7.1 in the papillomavirus composition.

However, Gajewski teaches that T cells require the participation of one additional "second signal", B7.1, to secrete IL-2. Gajewski also teaches that this aspect of cytotoxic T lymphocytes (CTL) would have a practical application in the development of tumor-specific immunotherapy, see the introduction on page 465. Expression of B7.1 human tumor cells can render them better able to stimulate alloreactive CD8+ lymphocytes to produce their own IL-2, see the first paragraph of the discussion section on page 470.

One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate B7.1 into the vaccinia composition used to treat papillomavirus infections taught by Stanley et al. or Borysiewicz et al. and Lin et al. to provide a co-factor stimulate T cells to secrete natural IL-2. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Stanley et al. and Hines et al. use immunostimulatory molecules in compositions to treat papillomavirus tumors and Gajewski teaches that B7.1 is useful for tumor-specific immunotherapy. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Applicant argues that none of the references teach the instant combination and that Gajewski, which is drawn to B7.1 tumor cells to treat cancer, does not suggest the inclusion of B7.1 in a vector.

Applicant's arguments have been fully considered, but are found unpersuasive because incorporating B7.1 in any of the vaccinia vectors taught by Stanley et al. or Borysiewicz et al. and Lin et al. would be an obvious alternative of expressing the protein. Further, papillomavirus causes cervical cancer and Gajewski teaches using B7.1 to treat cancer.

Claims 37, 63, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. Galloway, Borysiewicz et al., Lin et al. Hines et al. and Gajewski as applied to claims 32-36, 43, 44, 46-48, 53, 52-56, and 59-62 above, and further in view of Boursnell et al. (WO 92/16636).

The claims are drawn to the vaccinia vector expression is at the TK and/or K1L locus.

See the teachings of Stanley et al. Galloway, Borysiewicz et al., Lin et al., Hines et al. and Gajewski. None of the references teach vaccinia vector expression is at the TK and/or K1L locus.

However, Boursnell et al. teaches a recombinant vector that expresses wild-type or mutant portions of E6 and E7 from HPV16 and HPV18 for conditions caused by an HPV infection, see page 18, lines 1-4. Boursnell et al. teaches that using the Wyeth strain of the vaccinia virus as the vector had the lowest number of complications, see page 14, lines 17-25. The insertion of foreign DNA is favored at the thymadine kinase gene locus; see page 14, lines 26-28 and page 28, lines 22-26. Boursnell et al. also teaches that the p7.5 and/or the H6 promoters may be used, see page 16, lines 11-22.

One of ordinary skill in the art at the time the invention was made would have been motivated to use any gene locus of the Wyeth strain known in the art to encode the papillomavirus polypeptides to lower side effects that could be caused by administration of the vaccine, see Boursnell et al. on page 14, line 17 to page 15, line 12. One of ordinary skill in the art would have had a reasonable expectation for producing the claimed invention because Stanley et al. and Lin et al. use vaccinia to express the papillomavirus polypeptides and Borysiewicz et al. uses the Wyeth is a strain of vaccinia to treat papillomavirus infection.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Applicant argues that the references do not teach the claimed combination and the instant vector combinations are novel and inventive.

In response, the reference of Boursnell et al. is supplied to demonstrate obvious substitution for using different vaccinia vectors locuses. As applicant has pointed out, the Office must demonstrate that the references teach each limitation in the claims and the teachings of Boursnell et al. teach another limitation. In view of the teachings in the prior art, it is determined that the instant invention is not novel.

Claims 38, 64, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. Galloway, Borysiewicz et al., Lin et al. Hines et al. and Gajewski as applied to claims 32-36, 43, 44, 46-48, 53, 52-56, and 59-62 above, and further in view of Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038).

The claims are drawn to using MVA and inserting the DNA sequences encoding the papillomavirus vectors in excision regions of the virus.

See the teachings of Stanley et al. Galloway, Borysiewicz et al., Lin et al. Hines et al. and Gajewski above. None of the references teach using an MVA vector to express the proteins.

However, Meyer et al. teaches six major deletion sites in the wild-type vaccinia Ankara strain during attenuation to MVA that are not essential to viral replication and attenuate virus pathogenicity, see the abstract, the results section on page 1032-1034. In addition, Meyer et al. teaches that the insertion of the K1L gene of the MVA vaccinia strain leads to increased host range and suggests this as a selection system for recombinant viruses expressing foreign genes,

see page 1037, a third of the way down page 1037. Therefore, one of skill in the art at the time the invention was made would have been motivated to utilize the a vaccinia strain to express papillomavirus peptides, taught by Stanley et al., or Borysiewicz et al. and Lin et al., in a vaccine to treat the papillomavirus because of the large insertion areas provided by the non-essential viral genome that can be deleted without harming viral replication taught by Meyer et al. and to lower side effects that could be caused by administration of the vaccine, see Boursnell et al. on page 14, line 17 to page 15, line 12. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because Stanley et al. teaches how to express papillomavirus and immunostimulatory proteins in a vaccinia vector to treat papillomavirus infections and Meyer et al. uses a type of vaccinia virus that allows expression of large inserts. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Applicant argues that the invention is not the vector, but a vector expressing the claimed combinations.

As applicant has pointed out, the Office must demonstrate that the references teach each limitation in the claims and the teachings of Boursnell et al. teach another limitation. In view of the teachings in the prior art, it is determined that the instant invention is not novel.

Claims 40, 49-51, 57, 58, and 75-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. Galloway, Borysiewicz et al., Lin et al. Hines et al. and Gajewski as applied to claims 32-36, 43, 44, 46-48, 53, 52-56, and 59-62 above, and further in view of

Munger et al. (The EMBO Journal. 1989; 8: 4099-4105) and Crook et al. (Cell. 1991; 67: 547-556).

The claims are drawn to expressing non-oncogenic variants of the E6 and E7 papillomavirus polypeptides.

See the teachings of Stanley et al. Galloway, Lin et al., Hines et al. and Gajewski. Although Borysiewicz et al. teaches expressing a non-oncogenic form of E7, see the first full paragraph on page 1524, the reference does not teach the exact amino acids modified or modifying E6.

However, Crook et al. teaches loss of the wild-type tumor suppressor function is achieved by the expression of HPV-16, see the last paragraph of column 1 on page 547. Crook et al. also teaches that an amino acid mutation in E6 reduces binding to p53 by 94% by deleting amino acids 111-115. Munger et al. teaches that E7 disrupts the retinoblastoma (RB) tumor suppressor gene by forming a complex with RB, see the abstract on page 4099. Munger et al. also teaches that the amino acid sequences necessary to form the complex formation with RB is located at a small stretch of amino acids surrounding the cysteine residue at sequence position 24, see the last 2 sentences of the introduction on page 4099. One of ordinary skill in the art at the time of the invention would have been motivated to utilize the specific deletions taught by the references to significantly decrease or eliminate tumor suppression in these proteins. Further, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Stanley et al. Galloway, Lin et al. teach expressing the instant papillomavirus proteins in vaccinia vectors and Borysiewicz et al. teaches expressing a non-oncogenic version of E7 in a vaccinia vector to treat papillomavirus infections. The

combined references render the invention as a whole prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Applicant argues the invention is not drawn to the non-oncogenic variants, but the polypeptide combinations. Applicant also admit that the teachings if Munger et al. and Crook et al. were well known in the art at the time the invention as made and cites several citations in the disclosure.

Applicant's arguments as well as a review of the references have been fully considered, but are found unpersuasive. As evidenced by the teachings in the prior art, all of the required elements instantly claimed are taught, and the Office has demonstrated motivation to combine the individual elements and to expect success upon combining the elements. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SAF

Shanon Foley/SAF
June 28, 2002

James C. Housel

JAMES HOUSEL 7/1/02
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